B. In the Specification:

Please amend the specification as follows.

In the sections of text to be amended, text deleted from the original appears in ~~strikethrough~~ and text to be added to the original has been underlined. The Examiner's attention is drawn to the fact that numbers (that identify structures in the corresponding Figures) appearing in the original text were underlined and **bold**. In the requested amendment at page 28-29, a [bracket] set was used to indicate deleted text in the word "tritura[r]ted" because ~~strikethrough~~ might be difficult to read (See: 37 C.F.R. § 1.121(b)(1)(ii) for the use of brackets). Brackets are similarly being used to delete the text "··" after each occurrence of ($DMSOd_6$) at pages 29, 30, 31 and 36.

Please delete the text under the section entitled: "Cross Reference To Related Applications:" at page 2 of the application. No replacement text is supplied.

Please delete the section of text at page 14, lines 1-12 and insert therefore the following text:

With reference to Figure 3A and Example 8, the tert-butyldimethylsilyl (TBDMS) ester of $(^{18}O)_2$ bromoacetic acid (**14**) was used in the alkylation reaction. This ester was prepared using ^{18}O labeled bromoacetic acid (**13**), obtained as a custom order from Cambridge Isotope Laboratory, Inc., and TBDMS-CN. The TBDMS ester of N-methyl piperazine acetic acid (**15**) was the product of the alkylation with N-methyl piperazine. The TBDMS ester was selected so that it could be converted to the acid chloride with, for example, oxalyl chloride thereby avoiding the requirement for any water and the possible exchange of ^{18}O with ^{16}O. In the presence of solid phase base (ss-TBD) and N-hydroxysuccinimide (NHS), the acid chloride was converted to the NHS ester (**16**). If the carboxylic acid is desired, instead of the active ester, the TBDMS ester could be converted to the carboxylic acid by treatment with an anhydrous acid such as TFA. Accordingly, aqueous treatment that might lead to $^{18}O \Leftrightarrow {}^{16}O$ exchange, can be avoided whether ~~to~~ the active ester or the carboxylic acid is desired.

Please delete the section of text beginning at page 16, line 8 and ending at page 17, line 6 of the application and insert therefore the following text:

With reference to Figure 4A and Example 10, this procedure was used to prepare active esters of 2,2,2-trifluorethanol and 1,1,1,3,3,3-hexafluoro-2-propanol. According to the figure and the example, the phenyl ester of N-methyl piperazine acetic acid ~~(19)~~ (20) was treated with trimethyl silyl imidizole (TMS-imidizole) and sodium phenoxide to form the imidazolide of N-methyl piperazine acetic acid ~~(20)~~ (21). The imidazolide ~~(20)~~ (21) was then reacted with either 2,2,2-trifluorethanol or 1,1,1,3,3,3-hexafluoro-2-propanol to produce the desired active ester of N-methyl piperazine acetic acid ~~(21) or (22)~~ (22) or (23), respectively as a bis-acid salt.

In some other embodiments, the active ester can be prepared by conversion of the N-substituted piperazine acetic acid, including isotopically enriched versions thereof, to an acid chloride followed by subsequent reaction of the acid chloride with the alcohol of choice to thereby produce the active ester of the selected alcohol.

With reference to Figure 4B and Example 11, the preparation of the NHS and NHP esters of N-methyl piperazine acetic acid are illustrated using this general procedure. According to the figure and the example, N-methyl piperazine acetic acid is treated with oxalyl chloride to produce the acid chloride ~~(23)~~ (24). The acid chloride is then treated with either of NHP or NHS and solid phase base to thereby produce the active ester ~~(24) or (25)~~ (25) or (26), respectively as the free piperazine base (not as an acid salt).

Figure 4B also illustrates the application of oxalyl chloride to the production of the pentafluorophenyl (Pfp) ester ~~(26)~~ (27) wherein a solution phase base (e.g. triethylamine) is used. The reaction proceeded well with the solution phase base but the hydrochloride salt of the base proved difficult to remove. Application of the solid phase base avoids this caveat.

Please delete the section of text beginning at page 28, line 30 and ending at page 29, line 16 of the application and insert therefore the following text:

To a stirring solution of 1.18 g (11.83 mmol) N-methyl piperazine in 15 mL of toluene at room temperature was added 1 g (5.91 mmol) of ethylbromoacetate,1,2-^{13}C dropwise, over a period of 15 minutes. Immediate formation of white solid was observed. The reaction mixture was then heated in an oil bath at 90^{0}C for 4 hr. After cooling the

mixture to room temperature, the off-white solid was removed by filtration, and washed with 25 mL of toluene. The combined filtrate and washings was then concentrated in a rotoevaporator, and the residue was dried under high vacuum for 5 hours to yield 1.10 g (quantitative) of ethyl ester of N-methyl piperazine acetic acid-1, 2-^{13}C (**9**) as an off-white oil. The crude product (**9**) was analyzed by MS and ^{1}H-NMR, and was directly used for the next step without further purification. MS (ESI, m/z): 189.16 (M+1), ^{1}H-NMR ($DMSOd_6$) [··] $\underline{\delta}$ 4.2 (m, 2H), 3.4 (d,1H, J=7Hz), 3.05 (d,1H, J=7Hz)), 2.4-2.7 (b, 8H), 2.3 (s, 3H), 1.25 (t, 3H).

A solution of ethyl ester of N-methyl piperazine acetic acid (**9**) (1.1 g, mmol), prepared as described above, in water (20 mL) was refluxed for 24 hr. The reaction was monitored by MS analysis. After 24 hr, the reaction mixture was concentrated in a rotoevaporator to afford white solid product, which was tritura[r]ted with acetone (10 mL) overnight. The product was then separated by filtration and dried under high vacuum overnight at 45^{0}C in a vacuum oven, to yield 780 mg of N-methyl piperazine acetic acid, 1, 2-^{13}C (**10**), as a white powdery solid. 300mg of the product was further purified by sublimation (1mm/Hg, 110-120^{0}C) to yield 270 mg of white solid. MS (ESI, m/z): 161 (M +1), ^{1}H-NMR ($DMSOd_6$) [··] $\underline{\delta}$ 3.3 (d,1H, J=7Hz), 2.95(d, 1H, J=7Hz), 2.55-2.75 (b,4H), 2.3-2.45 (b,4H), 2.18 (s, 3H)

Please delete the section of text beginning at page 29, line 24 and ending at page 30, line 9 of the application and insert therefore the following text:

To a slurry of 200 mg (1.14 mmol) of N-methylpiperazine-^{15}N·2HCl (the ·2TFA salt can also be used) in methanol (MeOH, 14 mL), was added 1.76 g (4.59 mmol) of ss-TBD, with a loading of 2.6mmol/g, followed by CH_2Cl_2 (6 mL). The mixture was then sonicated for 15 minutes and was then cooled in an ice bath under an argon atmosphere. To this vigorously stirred slurry, a solution of 193 mg (1.14 mmol) of ethylbromoacetate-2-^{13}C in acetonitrile (3 mL) was added dropwise using a syringe pump (maintaining a rate of 2 mL/hr). After completion of the addition, the ice bath was removed and the mixture was continued stirring at room temperature overnight (18hr). The mixture was then filtered through a sintered funnel, and the solid was washed several times with MeOH (4X10 mL). The combined filtrate and washings were then concentrated in a rotoevaporator, and the

residue was kept under high vacuum to yield 111 mg (51%) of the ethyl ester of the N-methyl piperazine acetic acid (11) as an off white solid. This crude product was directly used for the next step without further purification. MS (ESI, m/z) 189 (M+1). ^{1}H-NMR (DMSOd_6) [··] δ 4.05 (q, 2H), 3.3(s,1H), 3.0 (s,1H), 2.4-2.5 (b, 4H), 2.2-2.4(b, 4H), 2.1 (s, 3H), 1.15 (t, 3H).

The product was hydrolyzed in the manner described in Scheme A, above. The following analytical data was obtained for the product.

MS (ESI, m/z) 161 (M+1). ^{1}H-NMR (DMSOd_8) [··] δ 3.35(s,1H), 3.05 (s,1H), 2.65-2.8(b, 4H), 2.5-2.65(b, 4H), 2.35 (s, 3H),

Please delete the section of text at page 31, lines 18-22 and insert therefore the following text:

To a solution of TBDMS-CN (172 mg, 1.190 mmol)) in DCM (0.575 mL) was added ^{18}O labeled bromoacetic acid (13) (170 mg, 1.189 mmol) under an argon atmosphere and the solution was heated to 80 °C for 20 minutes and then cooled to room temperature. The product (14) was isolated as an oil (254 mg, 85% yield). ^{1}H NMR ($CDCl_3$) [··] δ 3.58 (2H, -CH_2-), 0.955 (9H, (CH_3)$_3$-Si), 0.30 (6H, CH_3Si).

Please delete the section of text at page 33, lines 9-21 and insert therefore the following text:

To a solution of N-methyl piperazine phenyl ester ~~(19)~~ (20) (100 mg, 0.426 mmol) and sodium phenoxide (1mg, 9 μmol) in THF (5 mL) was added TMS-imidazole (69 μL, 0.468 mmol). The solution was mixed for 20 minutes to generate the imidazolide ~~(20)~~ (21). CF_3CH_2OH (80 μL, 0.213 mmol) was then added to the light yellow solution so obtained. The solution was mixed for another 30 minutes when TLC indicated clean formation of product (R_f = 0.6, 4:1 DCM-MeOH). The reaction was then diluted to 15 mL with EtOAc and the product ~~(21)~~ (22) was precipitated by addition of HCl solution in dioxane (4 M, 2mL). After washing with THF (2 x 15 mL) product was isolated as white solid. NMR of the solid indicated a 1:1 mixture of product and imidazole (as HCl salt). Calculated MH^+= 241.13, found = 241.12.

1,1,1,3,3,3-Hexafluoro-2-propanol ester ~~(22)~~ (23) was isolated using the general procedure set forth above provided however that $(CF_3)_2CHOH$ was substituted for CF_3CH_2OH. The following analytical data was obtained for this product. (R_f = 0.37, 9:1 DCM-MeOH). Calculated MH^+= 309.11 , found = 309.11.

Please delete the section of text beginning at page 33, line 28 and ending at page 34, line 2 of the application and insert therefore the following text:

To a suspension of N-methyl piperazine acetic acid (N-MPAA) (79 mg, 0.5 mmol) in DCM (25 mL) was added a solution of oxalyl chloride (4 mL, 0.8 mmol, 2.0 M solution in DCM) over 10 minute at room temperature. After another 30 minutes of reaction, solvent and excess reagent were removed under reduced pressure to give a white solid ~~(23)~~ (24). A solution of NHS (57 mg, 0.5 mmol) in DCM (25 mL) was added to the solid followed by ss-TBD (390 mg, 1 mmol, 2.6 mmol/g). The resulting solution was sonicated for 5 minute when all solid dissolved. The ss-TBD resin was removed by filtration and solvent was evaporated to yield a white foam (97% yield). Product was characterized by ES-MS as before.

Please delete the section of text at page 36, lines 16-30 and insert therefore the following text:

To a slurry of N-methyl piperazine acetic acid -1, 2-^{13}C, ^{18}O, 2·HCl ~~(27)~~ (28) (60 mg, 0.25 mmol) in THF (1.8 mL), was added DIPEA (98 mg , 0.76 mmol) under argon. The mixture was vortexed for 5 min, and the trifluoroacetate of N-hydroxysuccinimide (160 mg, 0.76 mmol) was added. After sonicating for 10 minutes, the reaction mixture was stirred at room temperature for 4 hours, followed by a centrifugation to remove any undissolved material. The supernatant was decanted then diluted with THF (3mL) and added slowly to a 4M solution of HCl in dioxane (1.8 mL). The precipitated HCl salt of the NHS-ester was separated by centrifugation, and washed with THF (3mL x 4), dried under high vacuum to yield 62 mg (74%) of the NHS ester ~~(29)~~ (30) as an off-white solid. MS (ESI, m/z) 261 (M+1), ^1H-NMR ($DMSOd_6$) [··] δ 4.05 (d,1H, J=7Hz), 3.7 (d,1H, J=7Hz), 3.3-3.45 (b, 2H), 2.95-3.1 (b, 2H), 2.85(s, 3H), 2.75 (m,4H).

With the exception of using a different isotopically enriched N-methyl piperazine acetic acid, the above describe procedure was followed for the production of the 115 labeling reagent ~~(30)~~ (31). The analytical data for the product ~~(30)~~ (31) is as follows.

MS (ESI, m/z) 261 (M+1). ^{1}H-NMR ($DMSOd_6$) [··] δ 4.05(s,1H), 3.7 (s,1H), 3.3-3.4 (b, 2H), 3.1-2.95(b, 4H), 2.85 (s, 3H), 2.75-2.80 (b, 1H), 2.7 (m, 4H).